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REMARKS

Claim 61 is pending in the subject application. By this Amendment, applicants have amended claim 61. Applicants note that the amendments to claim 61 are made to more clearly describe the claimed invention. Support for these amendments may be found in the instant specification on page 1, line 19 to page 2, line 3; page 2, lines 28-34; page 7, lines 3-30; Figure 1, page 26, lines 3-18; page 31, lines 15-28; page 34, lines 12-37; page 35, Table 2a; page 36, lines 17-39; and page 39, line 39 to page 41, line 8. Applicants maintain that these amendments to claim 61 raise no issue of new matter. Accordingly, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claim 61, as amended, will be pending and under examination.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 61 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that the reference to an agent that is "capable of binding", "capable of blocking", and "not capable of blocking" fails to adequately set forth the metes and bounds of the patent protection desired.

In response, but without conceding the correctness of the Examiner's ground of rejection, applicants note that, as amended, claim 61 recites that the agent "binds to a CCR5 chemokine receptor on the surface of the CD4+ cell", "blocks fusion of HIV-1_{JR-FL} with a PM-1 cell", and "does not block fusion of HIV-1_{BRU} with such PM-1 cell". Applicants maintain that these amendments obviate the Examiner's ground of rejection.

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In view of the remarks above, applicants maintain that claim 61, as amended, satisfies the requirements of 35 U.S.C. §112, second paragraph and request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner stated that claim 61 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In response to applicants' arguments set forth in the Amendment filed October 6, 2005, the Examiner stated that applicants had traversed this rejection and submitted that the pending claim is not directed toward an agent, but rather to a method of inhibiting macrophage tropic HIV-1 infection of CD4+ cells, suggesting that the written description criteria relied upon are not applicable.

The Examiner directed applicants to *University of Rochester v. G.D. Searle & Co., Inc* 358 F.3d 916, 69 U.S.P.Q.2d 1886 (CAFC 2004), wherein the court concluded that the written description requirement applies equally to product and method claims. The Examiner stated that the facts in this situation are similar to the facts in the instant application. The Examiner stated that applicants are claiming a method that employs a poorly defined agent. The Examiner stated that the agent is described solely in functional terms without any accompanying meaningful structural limitations.

The Examiner also stated that applicants argued that since the level of skill in the art was high at the time of filing this application, the level of disclosure required to meet the

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written description requirement is considerably less. The Examiner stated that he does not concur with this assessment. Specifically, citing Gait and Karn (1995), Richman (1996), Mellors (1996), and Back (1996), the Examiner stated that the design of HIV antiviral agents was a difficult undertaking.

The Examiner further stated that applicants argued that since applicants have provided a screening assay for identifying agents of the desired properties, they clearly were in possession of the claimed invention. The Examiner alleged that this argument is inapposite. Citing *University of Rochester v. G.D. Searle & Co., Inc.*, the Examiner stated that simply providing a generic methodology was insufficient to meet the written description requirement without some significant structural/functional nexus. The Examiner stated that simply having a screening assay does not allow the skilled artisan to readily envisage the structure of any given agent with the desired functional properties.

The Examiner noted that a Third Declaration by Dr. Dragic was submitted in support of applicants' arguments. The Examiner stated that Dr. Dragic argues that the level of skill in the art was very high at the time of filing as evidenced by the disclosed screening assay and identified agents that inhibit macrophage-tropic fusion. The Examiner further stated that Dr. Dragic also argued that a clear correlation was provided between the function and identifying characteristics of the claimed agent. The Examiner stated that these arguments are not persuasive for the reasons discussed *supra*.

In response, applicants again respectfully traverse the Examiner's rejection.

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The Examiner stated that applicants must be in possession of the claimed invention at the time of filing, and that although the skill in the art at the time of filing was high, so was its unpredictability.

In response, applicants maintain that as noted by the Examiner, the factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. On page 9 of the February 3, 2006 Office Action, the Examiner acknowledges that the level of skill in the biotechnology arts was high at the time of filing.

Applicants again maintain that the requirements for the disclosure to satisfy the written description requirements where the skill in the art is high is less than the requirements if the level of skill in the art was low. Applicants direct the Examiner's attention to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, Federal Register Vol. 66, No. 4, p. 1105, Section IIA(2), which states that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement." Accordingly, applicants maintain that the level of skill in the art at the time of filing does not require a more specific disclosure than applicants' disclosure since the knowledge in the art is such that one skilled in the art can read the instant disclosure and together with what is already known in the biotechnology arts, one skilled in the art can readily understand and envisage the

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claimed invention.

Applicants also maintain that the binding specificity of the agent and its functional properties, as recited in amended claim 61, i.e. blocking fusion of a PM-1 target cell with HIV-1_{JR-FL} but not blocking fusion of such PM-1 target cell with HIV-1_{BRU}, are unique identifying characteristics of the agent disclosed in the specification. Applicants further maintain that the property of the agent to bind to a CCR5 chemokine receptor on the surface of a CD4+ cell uniquely defines the agent. Moreover, applicants maintain that there is clearly a correlation between the function and the identifying properties of the agent.

Applicants also note that, as discussed below, the specification provides working examples of agents, for example, beta-chemokines, that satisfy the requirements recited in pending claim 61 as amended. Accordingly, applicants maintain that the specification contains an adequate written description and that the disclosure of the specification establishes that applicants were in possession of the claimed invention at the time of filing the instant application.

The Examiner stated that the disclosure fails to identify the molecular determinants on CCR5, CD4, and gp120 that mediate binding and virion-cell fusion, and that this would help the skilled artisan to identify putative subgenuses of inhibitory compounds.

In response, applicants maintain that the specification discloses the relationship of CCR5, CD4, and gp120 of HIV-1. As explained starting on page 36, line 17, CCR5 (known as C-C CKR-5 at the time), is the co-receptor with CD4 needed for HIV-1 entry into a cell. At page 36, lines 20-22, the specification states

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that "[i]t has been known for a decade that HIV-1 requires a second receptor for entry into CD4+ cells". As stated on page 36, lines 35-37, and as shown on page 37, Table 3, "[t]he expression of C-C CKR-5 on Hela-CD4 (human), COS-CD4 (simian) and 3T3-CD4 (murine) cells rendered each of them readily infectible by the primary, NSI strains ADA and BaL in the env-complementation assay of HIV-1 entry." Accordingly, applicants maintain that from reading the specification one skilled in the art readily understands that HIV-1 requires two receptors for entry into a CD4+ cell, the second receptor being CCR5, and that the blocking of HIV-1 gp120 binding to CCR5 would inhibit entry of HIV-1 into a CD4+ cell.

The Examiner further stated that the claim encompasses an inordinate number of compounds which are clearly not disclosed in the specification, and that, contrary to Dr. Dragic's assertion, the disclosure fails to provide guidance pertaining to the structure of the various subgenuses of inhibitory compounds.

In response, applicants point out that the specification discloses examples of various types of agents that provide guidance to the skilled practitioner as to the characteristics and functional properties of agents that satisfy the requirements recited in the pending claim as amended. Illustratively, beta-chemokines (see, *inter alia*, page 1, line 32 to page 2, line 3; page 2, lines 28-34; page 7, lines 3-30; Figure 1; page 26, lines 8-18; page 34, lines 33-37; and page 35, Table 2a), which satisfy the requirements of the pending claim, are described. The specification also discloses non-chemokine agents that block fusion of HIV-1_{JR-FL} with a PM-1 cell, but that do not block fusion of HIV-1_{BRU} with a PM-1 cell, including oligopeptides, polypeptides, antibodies or portions

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thereof, and nonpeptidyl agents (see page 14, lines 13-22; page 20, lines 22-27). The specification further discloses that antibodies to CCR5 block HIV-1 infection (see page 45, lines 33-35). Accordingly, applicants maintain that the specification teaches and exemplifies agents that meet the limitations of claim 61 as amended.

Applicants disagree with the Examiner's assertion that the disclosure fails to provide sufficient characteristics of the agent used in the claimed method. As stated in Dr. Dragic's Third Declaration, a person skilled in the art would readily conclude that the inventors had possession of the claimed invention. As Dr. Dragic stated, the specification discloses identifying characteristics of the agent utilized in the claimed method, namely, its specificity in binding to the CCR5 receptor; its ability to block fusion of a PM-1 target cell to HIV-1_{JR-FL}; and its inability to block fusion of a PM-1 target cell to HIV-1_{BRU}. Applicants again maintain that this teaching shows a clear correlation between the binding specificity to CCR5 and the identifying characteristics of the agent.

Finally, the Examiner stated that in *University of Rochester v. G.D. Searle & Co., Inc.*, the court clearly established that simply providing a generic methodology was insufficient to meet the written description requirement without significant structural/functional nexus.

Applicants disagree with the Examiner's assertion that the facts in *University of Rochester v. G.D. Searle & Co., Inc.* are very similar to those in the present case. Applicants assert that the claims at issue in *University of Rochester v. G.D. Searle & Co., Inc.* did not identify specific binding targets or any other properties of the compounds to be used in the claimed methods.

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The claims at issue in *University of Rochester v. G.D. Searle & Co., Inc.* only recited that such compounds "inhibit activity of the PGHS-2 gene product". In contrast, the presently amended claim recites an agent which inhibits infection of a CD4+ cell by a macrophage-tropic HIV-1 and further recites that this inhibition is accomplished by the agent's blocking fusion of the macrophage-tropic HIV-1 to the CD4+ cell through the binding of the agent to a CCR5 chemokine receptor on the surface of the CD4+ cell. The agent is further characterized in the claim as blocking fusion of HIV-1_{JR-FL} with a PM-1 cell; but not blocking fusion of HIV-1_{BRU} with such PM-1 cell.

Applicants maintain that the lack of identifying characteristics of the compounds in *University of Rochester v. G.D. Searle & Co., Inc.* does not exist in the subject application. This lack of identifying characteristics was central to the court's decision to affirm the decision of the district court finding that the written description requirement had not been met by the claims at issue in *University of Rochester v. G.D. Searle & Co., Inc.* Accordingly, this decision is distinguishable insofar as the Examiner is seeking to apply its holding to claim 61 as amended herein.

Regarding the disclosure of a method for identifying agents, i.e. the RET assay, applicants disagree with the Examiner's assertion that this assay is insufficient to show that applicants had possession of the claimed invention at the time of filing. Applicants maintain that the RET assay specifically identifies agents with the properties recited in amended claim 61, i.e. the binding specificity of the agent to the CCR5 receptor and the fact that the agent blocks fusion of a PM-1 target cell to one strain of HIV-1 (HIV-1_{JR-FL}) but does not block fusion of a PM-1 target cell to another HIV-1 strain (HIV-1_{BRU}).

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Applicants maintain that the RET assay disclosed is not merely a "generic methodology", but is a specific technique that identifies the agents described in the claimed method. Applicants assert that, based on the teaching of the instant disclosure, one skilled in the art can readily perform the disclosed RET screening assay to identify agents that satisfy the requirements of the agent specified in the pending claim. Applicants note that one skilled in the art is also provided with working examples of this assay as used to identify agents with the claimed functional activities (see, for example, pages 35-36, Table 2a and Table legend). Accordingly, the instant specification discloses agents that actually have the desired properties and effect, thus confirming that such agents are identified by the described RET assay.

In view of the foregoing remarks and arguments, applicants maintain that the specification as filed satisfies the written description requirements of 35 U.S.C. §112, first paragraph, with regard to claim 61 as amended herein and request that the Examiner reconsider and withdraw this ground of rejection.

Conclusion

Applicants maintain that in view of the remarks set forth above, the grounds of the Examiner's rejections have been overcome. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw these grounds of rejection of claim 61, and request allowance of this pending claim, as amended.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on forms PTO-SB08A and PTO-SB08B (substitute for form PTO-1449) attached hereto as **Exhibit A**.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(c)(2) before the mailing of a Final Office Action. Pursuant to C.F.R. §1.17(p) the fee for filing this Supplemental Information Disclosure Statement is \$180.00 and a check including this amount is enclosed.

In accordance with 37 C.F.R. §1.92(a)(2)(ii), copies of U.S. Patents and U.S. Patent Application Publications need not be provided. Accordingly, copies of documents listed below as items 1-54 are not submitted herewith. Copies of documents listed below as items 55-282 are attached hereto as **Exhibits 1-228**.

1. U.S. Patent No. 6,025,154 issued October 10, 2004 to Y. Li et al.;
2. U.S. Patent No. 6,265,184 issued July 24, 2001 to P.W. Gray et al.;
3. U.S. Patent No. 6,268,477 issued July 31, 2002 to P.W. Gray et al.;
4. U.S. Patent No. 6,448,375 issued September 10, 2002 to M. Samson et al.;
5. U.S. Patent No. 6,511,826 issued January 28, 2003 to Y. Li et al.;

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6. U.S. Patent No. 6,692,938 issued February 17, 2004 to M. Samson et al.;
7. U.S. Patent No. 6,743,594 issued June 1, 2004 to Y. Li et al.;
8. U.S. Patent No. 6,972,126 issued December 6, 2005 to G.P. Allaway et al.;
9. U.S. Patent No. 6,800,447 issued October 5, 2004 to M. Samson et al.;
10. U.S. Patent No. 6,800,729 issued October 5, 2004 to Y. Li et al.;
11. U.S. Patent No. 5,449,608 issued September 12, 1995 to N. Young et al.;
12. U.S. Patent No. 6,261,763 B1 issued July 17, 2001 to G.P. Allaway et al.;
13. U.S. Patent No. 6,528,625 issued March 4, 2003 to L. Wu et al.;
14. U.S. Patent No. 6,930,174 issued August 16, 2005 to M. Samson et al.;
15. U.S. Patent No. 6,100,087 issued August 8, 2000 to J. Rossi et al.;
16. U.S. Patent No. 5,939,320 issued August 17, 1999 to D. Littman et al.;

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17. U.S. Patent No. 6,258,527 issued July 10, 2001 to D. Littman et al.;
18. U.S. Patent No. 6,258,782 issued July 10, 2001 to S. Barney et al.;
19. U.S. Patent No. 6,692,938 issued February 17, 2004 to M. Samson et al.;
20. U.S. Patent No. 5,071,964 issued December 10, 1991 to M. Dustin et al.;
21. U.S. Patent No. 5,091,513 issued February 25, 1992 to J. Huston et al.;
22. U.S. Patent No. 5,215,913 issued June 01, 1993 to M.R. Posner et al.;
23. U.S. Patent No. 5,225,539 issued July 06, 1993 to G.P. Winter et al.;
24. U.S. Patent No. 5,603,933 issued February 18, 1997 to V.A. Dwyer et al.;
25. U.S. Patent No. 5,668,149 issued September 16, 1997 to S. Oroszlan et al.;
26. U.S. Patent No. 5,817,767 issued October 06, 1998 to G.P. Allaway et al.;
27. U.S. Patent No. 5,854,400 issued December 29, 1998 to T. Chang et al.;

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28. U.S. Patent No. 4,886,743 issued December 12, 1989 to L.E. Hood et al.;
29. Y. Li et al., U.S. Patent Application Publication No. 2003-0023044 published January 30, 2003;
30. P.W. Gray et al., U.S. Patent Application Publication No. 2005-0260565 published November 24, 2005;
31. P.W. Gray et al., U.S. Patent Application Publication No. 2005-0118677 published June 2, 2005;
32. L. Wu et al., U.S. Patent Application Publication No. 2003-0166870 published September 4, 2003;
33. C. Combadiere et al., U.S. Patent Application Publication No. 2004-0259785 published December 23, 2004;
34. C. Combadiere et al., U.S. Patent Application Publication No. 2003-0195348 published October 16, 2003;
35. D. Littman et al., U.S. Patent Application Publication No. 2003-0096221 published May 22, 2003;
36. L. Lopalco et al., U.S. Patent Application Publication No. 2003-0003440 published January 2, 2003;
37. P.W. Gray et al., U.S. Patent Application Publication No. 2002-0150888 published October 17, 2002;
38. M. Samson et al., U.S. Patent Application Publication No. 2004-0161739 published August 19, 2004;

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39. P.W. Gray et al., U.S. Patent Application Publication No. 2004-0230037 published November 18, 2004;
40. M. Samson et al., U.S. Patent Application Publication No. 2004-0110127 published June 10, 2004;
41. V. Roschke et al., U.S. Patent Application Publication No. 2005-0154193 published July 14, 2005;
42. V. Roschke et al., U.S. Patent Application Publication No. 2003-0100058 published May 29, 2003;
43. C. Rosen et al., U.S. Patent Application Publication No. 2003-0166024 published September 4, 2003;
44. Y. Li et al., U.S. Patent Application Publication No. 2004-0151719 published August 8, 2004;
45. Y. Li et al., U.S. Patent Application Publication No. 2001-0000241 published April 12, 2002;
46. V.M. Litwin et al., U.S. Patent Application Publication No. 2001-0046512 A1 published November 29, 2001;
47. C. Rosen et al., U.S. Patent Application Publication No. 2002-0048786 published April 25, 2002;
48. C. Rosen et al., U.S. Patent Application Publication No. 2002-0061834 published May 23, 2002;
49. M. Samson et al., U.S. Patent Application Publication No. 2002-0110870 published August 15, 2002;

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50. Y. Li et al., U.S. Patent Application Publication No. 2003-0023044 published January 30, 2003;
51. G.P. Allaway et al., U.S. Patent Application Publication No. 2006-0029932 published February 9, 2006;
52. G.P. Allaway et al., U.S. Patent Application Publication No. 2006-0140977 A1 published June 29, 2006;
53. G.P. Allaway et al., U.S. Patent Application Publication No. 2002-0045161 published April 18, 2002;
54. W.C. Olson et al., U.S. Patent Application Publication No. 2004-0062767 published April 01, 2004;
55. W.C. Olson et al., U.S. Patent Application Serial No. 11/451,707 filed June 12, 2006 (**Exhibit 1**);
56. W.C. Olson et al., U.S. Patent Application Serial No. 11/316,078 filed December 21, 2005 (**Exhibit 2**);
57. G.P. Allaway et al., U.S. Patent Application Serial No. 11/258,963 filed October 25, 2005 (**Exhibit 3**);
58. G.P. Allaway et al., U.S. Patent Application Serial No. 11/400,497 filed April 7, 2006 (**Exhibit 4**);
59. G.P. Allaway et al., U.S. Patent Application Serial No. 08/169,311, filed December 17, 1993 (now abandoned) (**Exhibit 5**);
60. G.P. Allaway et al., U.S. Patent Application Serial No. 08/475,515 filed June 7, 1995 (now abandoned) (**Exhibit 6**);

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61. V.M. Litwin et al., U.S. Patent Application Serial No. 08/587,458 filed January 17, 1996 (now abandoned) (**Exhibit 7**);
62. G.P. Allaway et al., U.S. Patent Application Serial No. 08/663,171 filed June 14, 1996 (now abandoned) (**Exhibit 8**);
63. V.M. Litwin et al., U.S. Patent Application Serial No. 09/118,415 filed July 17, 1998 (now abandoned) (**Exhibit 9**);
64. W.C. Olson et al., U.S. Patent Application Serial No. 09/464,902 filed December 16, 1999 (**Exhibit 10**);
65. D. Littman et al., U.S. Provisional Application No. 60/017,157, filed May 20, 1996 (**Exhibit 11**);
66. T. Dragic et al., U.S. Provisional Application No. 60/185,667 filed February 29, 2000 (**Exhibit 12**);
67. T. Dragic et al., U.S. Provisional Application No. 60/205,839 filed May 19, 2000 (**Exhibit 13**);
68. T. Dragic et al., U.S. Provisional Application No. 60/267,231 filed February 07, 2001 (**Exhibit 14**);
69. T. Dragic et al., U.S. Provisional Application No. 60/272,203 filed February 28, 2001 (**Exhibit 15**);
70. C. Combadiere et al., U.S. Provisional Application No. 60/018,508 filed May 28, 1996 (**Exhibit 16**);
71. PCT International Application Publication No. WO 92/01451, published 02/06/92 (**Exhibit 17**);

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72. PCT International Application Publication No. WO 95/16789
published June 22, 1995 (**Exhibit 18**);
73. PCT International Application Publication No. WO 97/28258
published August 7, 1997 (**Exhibit 19**);
74. PCT International Application Publication No. WO 97/44462
published November 27, 1997 (**Exhibit 20**);
75. PCT International Application Publication No. WO 98/18826
published May 07, 1998 (**Exhibit 21**);
76. PCT International Application Publication No. WO 01/55439,
published August 02, 2001 (**Exhibit 22**);
77. PCT International Application Publication No. WO 02/064612
published August 22, 2002 (**Exhibit 23**);
78. PCT International Application Publication No. WO 01/58915
published August 16, 2001 (**Exhibit 24**);
79. PCT International Application Publication No. WO 01/58916
published August 16, 2001 (**Exhibit 25**);
80. PCT International Application Publication No. WO 96/39437
published December 12, 1996 (**Exhibit 26**);
81. PCT International Application Publication No. WO 97/22698
published June 26, 1997 (**Exhibit 27**);
82. PCT International Application Publication No. WO 97/44055
published November 27, 1997 (**Exhibit 28**);

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83. PCT International Application Publication No. WO 97/032019
published September 4, 1997 (**Exhibit 29**);
84. European Patent Application No. 96870021.1 filed March 1,
1996 (**Exhibit 30**);
85. European Patent Application No. 96870102.9 filed August 6,
1996 (**Exhibit 31**);
86. European Patent Application Publication No. 1145721 A2
published October 17, 2001 (**Exhibit 32**);
87. European Patent Application Publication No. 1146055 A2
published October 17, 2001 (**Exhibit 33**);
88. European Patent Application Publication No. 1146122 A2
published October 17, 2001 (**Exhibit 34**);
89. European Patent Application Publication No. 1148126 A2
published October 24, 2001 (**Exhibit 35**);
90. European Patent Application Publication No. 1148127 A2
published October 24, 2001 (**Exhibit 36**);
91. European Patent Application Publication No. 1149582 A2
published October 31, 2001 (**Exhibit 37**);
92. European Patent Application Publication No. 1199360 A2
published April 24, 2002 (**Exhibit 38**);
93. European Patent Application Publication No. 1482042 A1
published December 1, 2004 (**Exhibit 39**);

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94. European Patent Application Publication No. 0815137 published December 12, 1996 (**Exhibit 40**);
95. European Patent No. 0883687 B1 issued November 27, 2004 (**Exhibit 41**);
96. Canadian Patent Application Publication No. 2216990 published December 27, 1997 (**Exhibit 42**);
97. Abaza, M.S.I et al., (1992) "Effects Of Amino Acid Substitutions Outside An Antigenic Site On Protein Binding To Monoclonal Antibodies Of Predetermined Specificity Obtained By Peptide Immunization: Demonstration With Region 94-100 (Antigenic Site 3) Of Myoglobin", *J. Prot. Chem.* 11(5):433-443 (**Exhibit 43**);
98. Alexander, H. et al., (1992) "Altering The Antigenicity Of Proteins", *Proc. Natl. Acad. Sci.* 89:3352-3356 (**Exhibit 44**);
99. Alkhatib et al., (1996) Abstract At 3rd Conference On Retroviruses (**Exhibit 45**);
100. Allan, J., (1997) "Human Immunodeficiency Virus-Related Infections In Animal Model Systems", In *AIDS: Biology, Diagnosis, Treatment And Prevention*, 4th Edition, Lippincott-Raven Publishers, Philadelphia, Pp 15-27 (**Exhibit 46**);
101. Allaway, G.P. et al., (1993) "Synergistic Inhibition Of HIV-1 Envelope-Mediated Cell Fusion By CD4-Based Molecules In Combination With Antibodies To gp120 Or gp41", *AIDS Res Hum Retroviruses* 9:581-587 (**Exhibit 47**);

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102. Allaway, G.P. et al., (1995) "Expression And Characterization Of CD4-IgG2, A Novel Heterotetramer That Neutralizes Primary HIV Type 1 Isolates", *AIDS Res Hum Retrovirus* 11:533-539 (**Exhibit 48**);
103. Amara, A. et al., (1997) "HIV Coreceptor Downregulation As Antiviral Principle: SDF-1-alpha-Dependent Internalization Of The Chemokine Receptor CXCR4 Contributes To Inhibition Of HIV Replication", *J. Exp. Med.* 186:139-146 (**Exhibit 49**);
104. Arthos, J. et al., (1989) "Identification Of The Residues In Human CD4 Critical For The Binding Of HIV". *Cell* 57:469-481 (**Exhibit 50**);
105. Ashorn, P.A. et al., (1990) "Human Immunodeficiency Virus Envelope Glycoprotein/CD4 Mediated Fusion Of Nonprimate Cells With Human Cells", *J. Virol.* 64:2149-2156 (**Exhibit 51**);
106. Attanasio, R. et al., (1991) "Anti-Idiotypic Antibody Response To Monoclonal Anti-CD4 Preparations In Nonhuman Primate Species", *J. Immunol.* 146:507-514 (**Exhibit 52**);
107. Baba, M. et al., (1988) "Mechanism Of Inhibitory Effect Of Dextran Sulfate And Heparin On Replication Of Human Immunodeficiency Virus *In Vitro*", *Proc. Natl. Acad. Sci.* 85:6132-6135 (**Exhibit 53**);
108. Baulerle, P.A. And Huttner, W.B., (1987) "Tyrosine Sulfation Is A Trans-Golgi-Specific Protein Modification", *Cell. Biol.* 105:2655-2663 (**Exhibit 54**);

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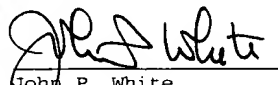
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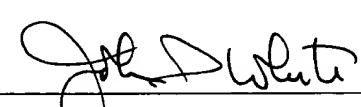
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No fee, other than the \$510.00 fee for a three-month extension
of time and the \$180.00 fee for filing the Supplemental
Information Disclosure Statement incorporated herein, is deemed
necessary in filing this Amendment. However, if any additional
fee is required, authorization is hereby given to charge the
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Respectfully submitted,

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